II. REMARKS

Claims 1-37 are pending. Pursuant to a Restriction Requirement, claims 1-16, 18, and 24-37 have been canceled. Examined claims 17 and 19-23 stand variously rejected under 35 U.S.C. § 112, first and second paragraphs. Applicants note with appreciation that previous rejections under 35 U.S.C. § 112, second paragraph and 35 U.S.C. § 102 have been withdrawn.

By amendment herein, claim 17 has been amended to indicate that the recombinant alphavirus particle contains one or more mutations (*e.g.*, substitutions, additions and/or deletions) at about amino acids 158 through 162 of the E2 glycoprotein, as compared to wild-type. Support for this amendment can be found throughout the specification as filed, for example, on page 5, lines 4 to 9.

In view of the foregoing amendments and following remarks, Applicant respectfully requests reconsideration of the restriction requirement and of the application.

Claim Objection/35 U.S.C. § 112, First Paragraph (New Matter)

Claim 17 was objected to and rejected under 35 U.S.C. § 112, first paragraph as allegedly containing new matter. (Final Office Action, page 2). Applicants submit that the Office has erred in determining the amendments raise issues of new matter. Indeed, it is well-settled that information contained in any one of the specification, claims or drawings of an application as filed may be added to any other part of the application without introducing new matter. See, e.g., M.P.E.P. 2163.06. The specification as filed clearly teaches that alphavirus particles that infect DC having amino acid mutations in the E2 glycoprotein. (See, *e.g.*, page 5, lines 4 to 9 stating "[w]ithin certain embodiments of the above, the alphavirus vector or recombinant alphavirus particle has an amino acid substitution in the E2 glycoprotein as compared to wild-type..." and page 5, lines 19 to 23 stating a "mutation (*e.g.*, substitution, deletion, or insertion, as compared to wild-type)..."). Thus, the previous amendments to the claims were fully supported by the specification as filed and did not constitute new matter.

Nonetheless, solely to expedite prosecution, Applicants have amended claim 17 herein to incorporate, verbatim, language from the specification as filed. Accordingly,

even though the previous amendment to claim 17 did not constitute the addition of new matter, the objection has been obviated.

35 U.S.C. § 112, Second Paragraph

Claim 17 stands rejected as allegedly unclear. In particular, it is maintained that it is unclear which amino acid is mutated. (Final Office Action, page 4). Although Applicants submit that the claims were sufficiently clear as filed (*e.g.*, any mutation in E1/E2 glycoprotein wherein the particle infects DC cells), the rejection has been obviated by the foregoing amendments. Accordingly, Applicants respectfully request withdrawal of the rejection.

35 U.S.C. § 112, First Paragraph, Enablement

Claims 17 and 21-23 stand rejected as allegedly not enabled by the specification as filed.

The Examiner makes several points in support of this rejection. First, Tucker and MacDonald are cited for indicating that mutations of an alphavirus render the virus more neurovirulent and/or may abolish the ability to infect DC cells. (Final Office Action, page 3). Second, the Examiner also cites Tucker for the proposition that mutations may cause severe problems in the host. (Final Office Action, page 3). Finally, it is asserted that the specification does not teach that an alphavirus having any other mutation than Gly at position 160 is able to infect DCs. (Final Office Action, page 3).

Applicants traverse the rejection and address the Examiner's points in turn.

As a threshold matter, Applicants again note that neither Tucker nor MacDonald bears any relevance to the pending claims. Neither Tucker nor MacDonald in any way address infection of human dendritic cells with alphaviruses - a major problem solved by Applicants. Indeed, both references are directed to infection of murine cells. As previously noted and discussed at length in the specification, "the ability of an alphavirus to efficiently infect murine dendritic cells is not predictive of its ability to efficiently infect human dendritic cells." (See, *e.g.*, page 25, lines 11-13 of the

specification). Accordingly, Tucker and MacDonald are not relevant to the claimed invention and in no way establish unpredictability.

With regard to the allegation that Tucker evidences that mutations can cause severe problems in a host, Applicants again note that the pending claims are directed to particles that infect human DC, while Tucker is limited entirely to infection of murine neuroblastoma cells and hamster kidney cells. Accordingly, the "problems" apparent in Tucker's cells may not arise in human host cells. Furthermore, Applicants remind the Examiner that the pending claims are not methods of treatment claims. As such, the question of the side-effects is immaterial. Even if the claims were directed to methods of using alphaviruses in a host, it is not the Patent Office's job to act as a regulatory agency in determining safety. Indeed, the question of safety is not relevant to an enablement inquiry. Rather, the inquiry remains what the specification teaches one of skill in the art. For the reasons detailed below, the pending claims are more than amply enabled by the specification as filed.

Finally, turning to what the specification teaches regarding mutations, Applicants strongly disagree with the Examiner's contention that only mutations at 160 are enabled. The Examiner incorrectly asserts that the enablement requirement necessitates multiple working examples of each and every embodiment encompassed by the claims. However, it is axiomatic that the scope of an applicant's claims is not limited to those embodiments which are actually exemplified in the specification. (*see, e.g., Spectra-Physics Inc. v. Coherent Inc.*, 3 USPQ2d 1737 (Fed. Cir. 1988)). The pending claims are directed to particles having mutations at about amino acids 158 to 162, as set forth throughout the specification. (See, page 5, lines 4-8). Also disclosed are methods of testing which mutants confer tropism for human dendritic cells. The teachings of the specification (including Examples) readily enable one of skill in the art to select and identify mutations affecting amino acids residues at about 158 to 162 of the E2 gene region) that confer the human dendritic cell tropic phenotype and incorporate said mutations into recombinant alphavirus particles.

Simply put, one skilled in the art would have no trouble in following Applicants' specification to make and test the embodiments falling within the scope of

the claims and undue experimentation would not be required to make and use the compositions as claimed. Accordingly, withdrawal of the rejection is in order.

III. CONCLUSION

For the reasons state above, Applicant respectfully submits that the pending claims define an invention which is novel and fully enabled by the specification. Accordingly, Applicant requests that the rejection of the claims be withdrawn, and that the application proceed to allowance.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 18-1648.

Please direct all further communications regarding this application to:

Anne S. Dollard, Esq.
CHIRON CORPORATION
Intellectual Property - R440
P.O. Box 8097
Emeryville, CA 94662-8097
Telephone: (510) 923-2719
Facsimile: (510) 655-3542

Respectfully submitted,

Date: 04 Sept 02

By: Dpasternak

Dahna S. Pasternak
Registration No. 41,411

CHIRON CORPORATION
Intellectual Property - R440
P.O. Box 8097
Emeryville, CA 94662-8097
Telephone: (650) 325-7812
Fax: (650) 325-7823

Version Showing Changes Made to Claims

17. (Twice Amended) A recombinant alphavirus particle which infects human dendritic cells, said recombinant alphavirus particle comprising one or more amino acid mutations [in the E1 or] at about amino acids 158 through 162 of the E2 [polypeptide] glycoprotein as compared to wild-type, with the proviso that said recombinant alphavirus particle is not derived from ATCC # VR-2526.

Currently Pending Claims

1 to 16. Withdrawn

17. (Twice Amended) A recombinant alphavirus particle which infects human dendritic cells, said recombinant alphavirus particle comprising one or more amino acid mutations at about amino acids 158 through 162 of the E2 glycoprotein as compared to wild-type, with the proviso that said recombinant alphavirus particle is not derived from ATCC # VR-2526.

18. Withdrawn.

19. The recombinant alphavirus particle of claim 17 or 18 wherein said alphavirus is a Sindbis virus.

20. The recombinant alphavirus particle according to claim 19 wherein said alphavirus has an amino acid substitution at E2 residue 160, as compared to wild-type Sindbis virus.

21. The recombinant alphavirus particle according to claim 17 or 18 wherein said alphavirus is Semliki Forest virus.

22. The recombinant alphavirus particle according to claim 17 or 18 wherein said alphavirus is Ross River virus.

23. The recombinant alphavirus particle according to claim 17 or 18 wherein said alphavirus is Venezuelan equine encephalitis virus.

24 to 37. Withdrawn.